

“WHEN THE TREATMENT STRIKES BACK: A CASE SERIES ON JARISCH HERXHEIMER REACTION IN SYPHILIS”

Dermatology

**Dr. M.G
Vijaikumar**

MD.DVL., Assistant Professor, Department Of Dermatology, Venereology And Leprosy, Government Sivagangai Medical College & Hospital, Sivagangai, Tamilnadu-630561

**Dr. S. Soundharyaa
Moorthi***

MD.DVL., Assistant Professor, Department Of Dermatology, Venereology And Leprosy, BGS Global Institute Of Medical Sciences, Bangalore-560060 *Corresponding Author

Dr. S. Seeniammal

MD.DVL., Assistant Professor, Department Of Dermatology, Venereology And Leprosy, Tirunelveli Medical College & Hospital, Tirunelveli, Tamilnadu-627011.

ABSTRACT

JHR is a rare febrile inflammatory reaction occurring after penicillin injections for spirochetal infections. Its usually mild and self-limiting condition and highly encountered with early syphilis than late syphilis. We present this rare case series of JHR encountered in three patients over a period of one month (March 2020) in Sexually Transmitted Infections (STI) clinic in Tirunelveli Medical College & Hospital. All three cases had high risk behaviour and JHR was seen in early syphilis (2 secondary & 1 early latent), with very high titres of RPR and TPHA positivity, thus proving that increased treponemal burden may be one possible trigger for JHR. The prognosis is so favorable with full recovery following supportive measures. The reaction might mimic disease progression or penicillin hypersensitivity, making differential identification crucial.

KEYWORDS

Syphilis, JHR, Penicillin, Spirochetes

INTRODUCTION:

The Jarisch- Herxheimer Reaction (JHR) is defined as a transient immunological reaction, classically seen in patients after antimicrobial treatment with penicillin for spirochetal infections, generally syphilis.

The other spirochetal infections encountering such reaction are leptospirosis, relapsing fever, Lyme's disease, etc.¹ It is also known as “Therapeutic Shock”. It is a delayed type of hypersensitivity reaction which exhibits all or none phenomenon. The classical signs of JHR include self-limiting 'flu-like syndrome', arthritis, vomiting, tachycardia, hypotension and exacerbation of existing cutaneous lesions and it typically settles within 12-24 hours.² Higher incidence of JHR (80-90%) is seen with early syphilis (primary, secondary & early latent syphilis) and infrequently in late syphilis except general paresis of insane where it can occur in 75% of patients.³

Though JHR is very common following penicillin injection, reportage of such reaction is very rare in current scenario probably due to decline in number of syphilis cases or misdiagnosis as penicillin hypersensitivity or negligence. We present this rare case series of JHR encountered in three patients during one month period (March 2020) in Sexually Transmitted Infections (STI) clinic in Tirunelveli Medical College & Hospital, Tamilnadu, India.

Case History:

Case 1:

A 28 years old unmarried male presented in Dermatology OPD with red coloured skin lesions all over the body for 10 days. The patient seems to be a homosexual with unprotected sex with unknown male through oro-insertive, ano-receptive, ano-insertive routes 45 days back. On dermatological examination, multiple erythematous scaly papules and annular scaly plaques were seen over shaft of penis, scrotum, trunk, abdomen, perianal region, palms and soles. (Figure 1A) He was uncircumcised. He had bilateral inguinal and femoral lymphadenopathy. Other cutaneous areas were found to be normal. Diagnosis of secondary syphilis was made based on RPR (Rapid Plasma Reagin) positivity- 1:256 dilution and TPHA (Treponema Pallidum Haemagglutination) positivity and he was negative for HIV. The patient was treated with single dose of injection Benzathine penicillin 2.4 million units IM after test dose.

After 3 hours post treatment, patient had fever, sweating, hypotension, exacerbation of existing cutaneous lesions and few new erythematous macules & papules occurred over the trunk, abdomen & scrotum. (Figure 1B) It seemed to be a severe JHR following penicillin injection and so the patient was treated with Inj. hydrocortisone 100mg IV stat + Inj. chlorpheniramine maleate 2cc IM stat, antipyretics and IV fluids. Following rescue measures, the patient became normal within 8 hours.

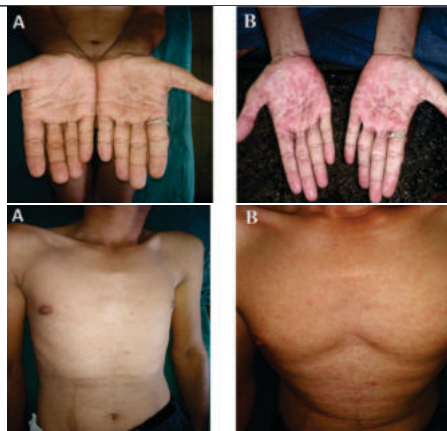


Figure 1: A case of **secondary syphilis** with multiple annular scaly papules and plaques over both palms and trunk (A) Before penicillin injection (B) Exacerbation of lesions after 3 hours of penicillin injection

Case 2:

A 22 years old unmarried male came for STI screening with high-risk behaviour of Men who have Sex with Men (MSM) contact with an unknown male, unprotected, ano-receptive, ano-insertive 3 months back. Dermatological examination was completely normal with no genital ulcer/discharge/scar. There was no inguinal lymphadenopathy, bones and joints, oral mucosa, palms and soles were all normal. Routine STI screening was done and he was found to be reactive for syphilis with RPR-1:128 dilution and TPHA positive. ICTC was found to be non-reactive. Patient was diagnosed as early latent syphilis and was treated with single dose of benzathine penicillin injection 2.4 million units IM after test dose. Later after 4 hours of treatment, patient had developed fever, headache, hypotension and sweating. It was found to be a mild JHR following penicillin administration. Patient was given supportive care, adequate fluids & NSAIDs and the patient was completely normal after 4 hours.

Case 3:

A 30 years old married male presented in Dermatology OPD with dark coloured skin lesions over both palms and soles for 2 weeks. He had unprotected sex with unknown male (MSM), oro-insertive, ano-receptive, ano-insertive 2 months back. On examination, he was uncircumcised and no genital ulcer/discharge/scar was seen. Multiple dusky erythematous to hyperpigmented annular scaly papules and plaques were present over both palms and soles. (Figure 2A) Bilateral inguinal lymphadenopathy was present. Oral mucosa, scalp & hair,

bones & joints were found to be normal. He was diagnosed as secondary syphilis based on clinical presentation, reactive RPR (1:256 dilution) and TPHA positivity. ICTC was non-reactive. Treatment was with intramuscular injection with benzathine penicillin 2.4 million units after test dose. After 6 hours of treatment, patient developed fever, sweating, malaise, headache and existing annular lesions became swollen over both palms and soles. (Figure 2B) Patient also developed new annular lesions over face and soles. Confirmed as severe JHR following penicillin and so was treated with Inj.hydrocortisone 100mg IV stat+ Inj.chlorpheniramine maleate 2cc IM stat. The patient was absolutely fine after 6 hours.



Figure 2: A case of **secondary syphilis** with multiple dusky erythematous to hyperpigmented annular scaly papules and plaques over both palms and soles (A) Before penicillin injection (B) Exacerbation of lesions after 6 hours of penicillin injection

DISCUSSION:

JHR is a rare febrile inflammatory reaction occurring after penicillin injections for spirochetal infections and JHR signals a rapid immune response to spirochete destruction, reinforcing that the antibiotic is acting effectively. The time of reaction varies from 2 to 12 hours post penicillin injection in each individual. JHR is thought to have multifactorial pathogenesis and the most common one explained was the breakdown of spirochete after antibiotic administration causing the release of toxins and cytokines. There is an increase in inflammatory cytokines like interleukin-6, interleukin-8 and tumour necrosis factor-alpha (TNF-alpha) accountable to such inflammatory reaction.⁴

In our study, JHR was seen in early syphilis (2 secondary & 1 early latent), with very high titres of RPR and TPHA positivity, thus proving that increased antigenic load (treponemal burden) may be one possible trigger for JHR. All 3 cases had high risk behaviour of Men having Sex with Men (MSM) with common signs of JHR like fever, hypotension, sweating and the two secondary syphilis patients had new similar lesions and exacerbation of existing cutaneous lesions as mentioned in the literature.⁵ A study done in Brazil with 115 syphilitic patients had JHR in only 10 cases and it showed increased incidence in secondary and early latent syphilis similar to our study and no such reaction in primary or tertiary disease.⁶ JHR is usually self-limiting necessitating fluid management and short course of NSAIDs. But, in severe reaction and in cases of neurosyphilis and cardiovascular syphilis, steroids are highly indicated.⁷

CONCLUSION:

The occurrence of JHR in this rare presentation underscores its diagnostic and prognostic significance, emphasizing the need for clinician awareness to avoid misinterpretation with penicillin hypersensitivity and to ensure appropriate management. The seriousness of this reaction mandates proper education and communication to patients and coordination among multiple specialty doctors.

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